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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,896	08/08/2001	Dennis W. Metzger	1954.1002-009	3394

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	8

DATE MAILED: 03/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/924,896	Metzger et al.
Examiner	**Art Unit**
Shin-Lin Chen	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 11, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above, claim(s) *1-7, 9-15, 17-19, 21-23, and 25-29* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *8, 16, 20, and 24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election of group II, claims 8, 16, 20 and 24, in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MEP. § 818.03(a)).

2. Claims 1-7, 9-15, 17-19, 21-23 and 25-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 7.

Claims 1-29 are pending and claims 8, 16, 20 and 24 are under consideration.

Claim Objections

3. Claims 8, 16, 20 and 24 are objected to because of the following informalities: Claims 8, 16, 20 and 24 depend on non-elected claims 1, 9, 17, and 21, respectively. Rewriting claims 8, 16, 20 and 24 as independent claims would be remedial. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 8, 16, 20 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 8 and 16 are directed to a method of inducing or enhancing an immune response to a T-cell independent (TI) antigen in a host comprising administering to the host the TI antigen and a polynucleotide encoding IL-12. Claim 20 is directed to a method of inducing an immune response to *Streptococcus pneumoniae* in a host comprising administering to the host the TI antigen of *Streptococcus pneumoniae* and a polynucleotide encoding IL-12. Claim 24 is directed to a method of inducing an immune response to *Neisseria meningiditis* in a host comprising administering to the host the TI antigen of *Neisseria meningiditis* and a polynucleotide encoding IL-12.

The specification only discloses the use of IL-12 protein and a TI antigen for inducing or enhancing an immune response to a TI antigen in a host. The claims encompass using a TI antigen and a polynucleotide encoding an IL-12 protein to induce or enhance an immune response to a TI antigen in a host, or using a corresponding TI antigen and polynucleotide encoding an IL-12 protein to induce an immune response to *Streptococcus pneumoniae* or *Neisseria meningiditis* in a host.

The specification fails to provide adequate guidance and evidence for how to use the polynucleotide or vector expressing IL-12 protein in combination with a TI antigen to induce or

enhance an immune response to a TI antigen in a host, or to induce an immune response to *Streptococcus pneumoniae* or *Neisseria meningiditis* in a host via various administration routes of said polynucleotide. The specification fails to provide adequate guidance and evidence for whether sufficient polynucleotide or vector encoding IL-12 protein would be present in target site of the host such that sufficient IL-12 protein is obtained to induce or enhance immune response to a TI antigen in a host, or to induce an immune response to *Streptococcus pneumoniae* or *Neisseria meningiditis* in a host via various administration routes of said polynucleotide.

The claims read on gene therapy by using a polynucleotide or any vector expressing IL-12 protein via various administration routes *in vivo*. The state of the art for gene therapy was unpredictable at the time of the invention. While progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired tissues *in vivo* continues to be unpredictable and inefficient as supported by numerous teachings available in the art. For example, Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicates that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Eck et al., 1996 (Goodman & Gilman's The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, p. 77-101) states that the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, and the rate of degradation of the

DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced are all important factors for a successful gene therapy (e.g. bridging pages 81-82).

In addition, Gorecki, 2001 (Expert Opin. Emerging Drugs, 6(2): 187-198) reports that "the choice of vectors and delivery routes depends on the nature of the target cells and the required levels and stability of expression" for gene therapy, and obstacles to gene therapy *in vivo* include "the development of effective clinical products" and "the low levels and stability of expression and immune responses to vectors and/or gene products" (e.g. abstract).

There is no evidence of record that administration of a TI antigen and a polynucleotide or vector expressing IL-12 protein to a host via various administration routes would result in sufficient expression of IL-12 protein at target site so as to provide therapeutic effects, such as inducing or enhancing an immune response to a TI antigen, or inducing an immune response to *Streptococcus pneumoniae* or *Neisseria meningiditis*, in a host. In view of the unpredictability of gene therapy *in vivo* and the lack of evidence of inducing or enhancing immune response to a TI antigen or inducing immune response to *Streptococcus pneumoniae* or *Neisseria meningiditis* in a host by using a polynucleotide or vector expressing IL-12 protein via various administration route, one skilled in the art at the time of the invention would not know how to use the TI antigen and a polynucleotide or vector expressing IL-12 protein to practice the claimed invention.

For the reasons discussed above, it would have required undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention claimed. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the working examples provided and scarcity of guidance in the specification, and the unpredictable nature of the art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.